16

37 C.F.R. §§ 1.821-1.825.

The following specific changes to the specification and claims are made by these amendments:

(a) The application as filed used a single SEQ ID NO to refer to both of the nucleotide sequence and the amino acid sequence for each of the first six sequences (*i.e.*, former SEQ ID NOS:1-6). Separate sequence identification numbers now have been provided for the nucleotide sequences and the corresponding amino acid sequences. For example, by these amendments, the nucleotide sequence for former SEQ ID NO:1 remains identified as SEQ ID NO:1, the amino acid sequence of former SEQ ID NO:1 is now identified as SEQ ID NO:2, the nucleotide sequence for former SEQ ID NO:2 is now identified as SEQ ID NO:3, the amino acid sequence for former SEQ ID NO:2 is now identified as SEQ ID NO:4, etc.

(b) FaNaCh, MEC-4, ASIC and MDEG sequences disclosed in Fig. 2 have been identified by SEQ ID NOs: 13, 14, 2 and 6, respectively.

(c) Primers listed on pages 15 and 16 have been identified by SEQ ID NOs: 15-18.

Accordingly, no new matter has been added.

Applicants respectfully submit that upon entry of the foregoing amendments, the application will conform to the

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requirements of 37 CFR §§ 1.821-1.825, and thus, it is in condition for examination.

Respectfully submitted,

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WEISER & ASSOCIATES, P.C.
Attorney for Applicants

Enclosures:
Replacement Sequence Listing - pages 1-34
Sequence Listing on diskette
Statement To Support Filing and Submission In Accordance With 37 C.F.R. §§ 1.821-1.825
Notice to File Missing Parts of Application

* * * * *

Certification Under 37 CFR 1.8

Date of Deposit 1-29-99

I hereby certify that this paper or fee is being deposited with the United States Postal Service with sufficient postage as first class mail under 37 CFR 1.8 on the date indicated above and is addressed to the Commissioner of Patents and Trademarks, Washington, D.C. 20231.

Kim Sheehan
(Name of person mailing)

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(Signature of person mailing)

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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Art Unit : 1646
Examiner : N. Basi
Serial No. : 09/129,758
Filed : August 5, 1998
Inventors : Rainer Waldmann
: Frederic Bassilana
: Eric Lingueglia
: Michel Lazdunski
: Catherine Heurteaux
: Antoine Champigny
Title : MAMMAL NEURONAL ACID
: SENSING CATIONIC CHANNEL,
: CLONING AND APPLICATIONS
: THEREOF

Docket No.: 1099-00

Date: November 2, 2001

17/C
A.J.J
2/15/02

AMENDMENT

Commissioner for Patents
Washington, D.C. 20231

Sir:

In response to the Official Action dated October 2, 2001, Applicants amend as follows:

Marked-Up Version Showing Changes Made to Specification

On page 7, first paragraph:

A DNA molecule comprising the sequence coding for the ASIC1B protein is that of 3647 ~~pb~~bp represented in the annexed list of sequences under number SEQ ID NO: 7 or its complementary sequence. More specifically, the invention relates to the nucleic sequence comprised between nucleotides 109 and 1785 of the sequence represented in the annexed list of sequences under number SEQ ID NO: 7 or its complementary sequence.

On page 7, second paragraph:

A DNA molecule coding for the DRASIC protein is that of 1602 ~~pb~~bp represented in the annexed list of sequences under number SEQ ID NO: 9 or its complementary sequence.

On page 7, third paragraph:

A DNA molecule coding for the~~MDEG1~~MDEG2 protein is that of 1602 ~~pb~~bp represented in the annexed list of sequences under number SEQ ID NO: 11 or its complementary sequence.

Paragraph bridging Pages 11 and 12:

Other characteristics and advantages of the invention will be seen in the description below related to research activities that led to the demonstration and the characterization of the ASIC channel, and in which reference will be made to the annexed sequences and drawings in which:

- SEQ ID NO: 2 represents the sequence of 526 amino acids of the protein of the ASIC channel deduced from the cDNA sequence of the rat (SEQ ID NO: 1).

- SEQ ID NO: 4 represents the partial sequence of 514 amino acids of the protein of the ASIC channel deduced from the partial sequence of human cDNA (SEQ ID NO: 3).

- SEQ ID NO: 6 represents the sequence of 512 amino acids of the protein of the MDEG channel deduced from the sequence of human cDNA (SEQ ID NO: 5).

- SEQ ID NO: 8 represents the sequence of 559 amino acids of the protein of the ASIC1B channel as well as the sequence of a DNA molecule comprising the sequence coding for that protein (SEQ ID NO: 7).

- SEQ ID NO: 10 represents the sequence of 533 amino acids of the protein of the DRASIC channel and the sequence of DNA coding for that protein (SEQ ID NO: 9).

- SEQ ID NO: 12 represents the sequence of 563 amino acids of the protein of the MDEG2 channel as well as the sequence of a DNA molecule comprising the sequence coding for that protein (SEQ ID NO: 11).

Marked-Up Version to Show Changes Made to the Claims

3) (Amended) Protein according to ~~one of claims~~claim 1 ~~or 2~~, the amino acid sequence of which is ~~represented in the annexed list of sequences under number~~ SEQ ID NO: ~~2~~4 or a functionally equivalent derivative of this protein.

11) (Amended) Nucleic acid molecule comprising ~~or constituted by~~ a nucleic sequence coding for a protein constituting a cationic channel according to one of claims 1 ~~to 6 or a hybrid channel according to one of claims 7 to 9~~, 2, 3 and 5.

17) (Amended) Vector comprising at least one nucleic acid molecule according to ~~one of claims~~claim 11 ~~to 16~~, advantageously combined with control sequences.

18) (Amended) Method for producing a protein constituting an ionic channel according to one of claims 1 ~~to 6 or a hybrid channel according to one of claims 7 to 9, characterized in that it comprises~~, 2, 3 and 5 comprising the steps of:

- transferring a nucleic acid molecule ~~according to one of claims 11 to 16~~comprising a nucleic acid sequence encoding a protein constituting a cationic channel according to one of claims 1, 2, 3 and 5 or a vector ~~according to claim 17~~comprising said nucleic acid molecule into a cell host,

- culturing said cell host under conditions allowing production of the protein constituting the ionic channel,

- isolating by any suitable means the proteins constituting the ionic channels.

19) (Amended) Method for expressing a protein constituting an ionic channel according to one of claims 1 ~~to 6 or a hybrid channel according to one of claims 7 to 9, characterized in that it comprises~~, 2, 3 and 5 comprising the steps of:

- transferring a nucleic acid molecule ~~according to one of claims 11 to 16~~comprising a nucleic acid sequence encoding a protein constituting a cationic channel according to one

of claims 1, 2, 3 and 5 or a vector ~~according to claim 17~~comprising said nucleic acid molecule into a cell host,

- culturing said cell host under conditions allowing production of the protein constituting the ionic channel.

20) (Amended) Method according to ~~one of claims~~claim 18 ~~or 19~~, ~~characterized in that~~wherein the cell host is selected from among the prokaryotes or the eukaryotes and notably from among the bacteria, yeasts or cells of mammals, plants or insects.

21) (Amended) Transformed cell expressing the mammalian neuronal amiloride-sensitive proton-activated cationic channels obtained by the method according to ~~one of claims~~claim 18~~to 20~~.

22) (Amended) Method for screening substances that are capable of modulating the activity of mammalian neuronal ionic channels, ~~characterized in that~~comprising contacting variable quantities of a substance to be tested ~~are brought into contact~~ with the cells according to claim 21 ~~then~~and measuring, using any suitable means, ~~one measures~~ the ~~possible~~ effects of said substance on the currents of the amiloride-sensitive proton-activated cationic channels.

23) (Amended) Method according to claim 22, ~~applied to the screening of substances~~wherein said substance is capable of modulating the perception of acidity, with regard to nociception ~~as well as~~and taste transduction.

24) (Amended) Pharmaceutical composition comprising as active ingredient at least one protein constituting an ionic channel according to one of claims 1 ~~to 6 or a hybrid channel according to one of claims 7 to 9~~, 2, 3 and 5 or an antibody ~~according to claim 10~~directed against said protein.

Please add the following new claims:

26) (New) Method according to claim 19, wherein the cell host is selected from among the prokaryotes or the eukaryotes and notably from among the bacteria, yeasts, or cells of mammals, plants, or insects.

27) (New) Transformed cell expressing the mammalian neuronal amiloride-sensitive proton-activated cationic channels obtained by the method of claim 19.

28) (New) Method for screening substances that are capable of modulating the activity of mammalian neuronal ionic channels, comprising contacting variable quantities of a substance to be tested with the cells according to claim 27 and measuring, using any suitable means, the effects of said substance on the currents of the amiloride-sensitive proton-activated cationic channels.

29) (New) Method according to claim 28, wherein said substance is capable of modulating the perception of acidity, with regard to nociception and taste transduction.

Please cancel Claims 4, 6-10, 14, 16 and 25 without prejudice and without disclaimer of the subject matter contained therein.

Marked-Up Version Showing Changes Made to the Abstract

~~The invention relates to a~~A protein constituting a mammalian neuronal cationic channel that is sensitive to amiloride and activated by protons, as well as the nucleic acid molecules coding this protein~~:~~; and ~~The invention also relates to a~~ method for screening substances that are capable of modulating the activity of mammalian neuronal ionic channels.

Remarks

In accordance with the response filed July 9, 2001, Applicants have elected Group I including Claims 1-3, 5, 11-13, 15 and 17-24 drawn to ASIC1 for prosecution. This response confirms that election. The Specification has been amended to correct a few minor typographical errors. The Claims have been amended to reflect the election of July 9, 2001. Claims 4, 6-10, 14, 16 and 25 are cancelled without prejudice and without disclaimer of the subject matter contained therein. Claims 3, 11, and 17-24 have been revised to proper multiple dependent form, thus necessitating the addition of Claims 26-29. No new matter has been added.

Claims 1-3, 5, 11-13, 15, 17-24 and 26-29 are present in the case.

To insure a complete record, we respectfully traverse the allegation that the response filed July 9, 2001 was not fully responsive to the Office Action dated May 11, 2001. According to 37 C.F.R. §1.111, to be fully responsive, "[t]he reply by the applicant or patent owner must be reduced to a writing which distinctly and specifically points out the supposed errors in the examiner's action and must reply to every ground of objection and rejection *in the prior Office Action.*"

The Official Action dated May 11, 2001 required only an election "to a single invention to which the claims must be restricted" as represented by Groups I-VI. Specifically, "Applicant is advised that the reply to this requirement to be complete must include an election of the invention to be examined even though the requirement be traversed (37 C.F.R. §1.143)". Thus, to be fully responsive to the Official Action, the Applicant needed only to elect an invention as defined by one of Groups I-VI.

Applicant's response dated July 9, 2001 did exactly what was required by the Official Action. Specifically, Applicants elected "Group I including Claims 1-3, 5, 11-13, 15 and 17-24 for immediate prosecution." No further action on the part of the Applicant was required

to be fully responsive to the Official Action dated May 11, 2001. In any event, this response is intended to address all issues that may be present to advance the application towards examination on the merits.

We respectfully submit that Claims 1-3, 5, 11-13, 15 and 17-24 of elected Group I contain the correct SEQ ID NOs corresponding to the sequence listing submitted on January 29, 1999 in response to the Notice of Missing Parts. The Official Action dated May 11, 2001 acknowledged the Amendment filed January 29, 1999 and based a new restriction requirement on the claims as amended therein. Thus, the amendments to the Application contained therein have presumably been entered so that the Specification and Claims contain the correct SEQ ID NOs in accordance with the revised sequence listing.

For the record, the claims of elected Group I are directed to ASIC1. Specifically, SEQ ID NO: 1 corresponds to rat ASIC1A DNA; SEQ ID NO: 2 represents rat ASIC1A protein; SEQ ID NO: 3 corresponds to human ASIC1A DNA; SEQ ID NO: 4 represents human ASIC1A protein; SEQ ID NO: 7 corresponds to rat ASIC1B DNA; and SEQ ID NO: 8 represents rat ASIC1B protein, as explained in the Specification at pages 2-3 as revised by the Amendment dated January 29, 1999.

Please note that a copy of the Amendment and Submission of Sequence Listing under 37 CFR 1.821 filed January 29, 1999 is enclosed herewith.

In light of the foregoing, we respectfully submit that the elected claims of Group I are in proper form for consideration on the merits, which early action we hereby urge.

Respectfully submitted,

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In the Specification (clean copy as amended)

On page 7, first paragraph:

A DNA molecule comprising the sequence coding for the ASIC1B protein is that of 3647 bp represented in the annexed list of sequences under number SEQ ID NO: 7 or its complementary sequence. More specifically, the invention relates to the nucleic sequence comprised between nucleotides 109 and 1785 of the sequence represented in the annexed list of sequences under number SEQ ID NO: 7 or its complementary sequence.

C1

On page 7, second paragraph:

A DNA molecule coding for the DRASIC protein is that of 1602 bp represented in the annexed list of sequences under number SEQ ID NO: 9 or its complementary sequence.

C2

On page 7, third paragraph:

A DNA molecule coding for the MDEG2 protein is that of 1602 bp represented in the annexed list of sequences under number SEQ ID NO: 11 or its complementary sequence.

C3

Paragraph bridging Pages 11 and 12:

Other characteristics and advantages of the invention will be seen in the description below related to research activities that led to the demonstration and the characterization of the ASIC channel, and in which reference will be made to the annexed sequences and drawings in which:

C4

- SEQ ID NO: 2 represents the sequence of 526 amino acids of the protein of the ASIC channel deduced from the cDNA sequence of the rat (SEQ ID NO: 1).

- SEQ ID NO: 4 represents the partial sequence of 514 amino acids of the protein of the ASIC channel deduced from the partial sequence of human cDNA (SEQ ID NO: 3).

- SEQ ID NO: 6 represents the sequence of 512 amino acids of the protein of the MDEG channel deduced from the sequence of human cDNA (SEQ ID NO: 5).

- SEQ ID NO: 8 represents the sequence of 559 amino acids of the protein of the ASIC1B channel as well as the sequence of a DNA molecule comprising the sequence coding for that protein (SEQ ID NO: 7).

C4 - SEQ ID NO: 10 represents the sequence of 533 amino acids of the protein of the DRASIC channel and the sequence of DNA coding for that protein (SEQ ID NO: 9).

- SEQ ID NO: 12 represents the sequence of 563 amino acids of the protein of the MDEG2 channel as well as the sequence of a DNA molecule comprising the sequence coding for that protein (SEQ ID NO: 11).

In the Claims (as amended)

13) (Amended) Protein according to claim 1, the amino acid sequence of which is SEQ ID NO: 4 or a functionally equivalent derivative of this protein.

11) (Amended) Nucleic acid molecule comprising nucleic sequence coding for a protein constituting a cationic channel according to one of claims 1, 2, 3 and 5.

17) (Amended) Vector comprising at least one nucleic acid molecule according to claim 11, advantageously combined with control sequences.

18) (Amended) Method for producing a protein constituting an ionic channel according to one of claims 1, 2, 3 and 5 comprising the steps of:

- transferring a nucleic acid molecule or a vector comprising said nucleic acid molecule into a cell host,

- culturing said cell host under conditions allowing production of the protein constituting the ionic channel,

- isolating by any suitable means the proteins constituting the ionic channels.

19) (Amended) Method for expressing a protein constituting an ionic channel according to one of claims 1, 2, 3 and 5 comprising the steps of:

- transferring a nucleic acid molecule comprising a nucleic acid sequence encoding a protein constituting a cationic channel according to one of claims 1, 2, 3 and 5 or a vector comprising said nucleic acid molecule into a cell host,

- culturing said cell host under conditions allowing production of the protein constituting the ionic channel.

20) (Amended) Method according to claim 18, wherein the cell host is selected from among the prokaryotes or the eukaryotes and notably from among the bacteria, yeasts or cells of mammals, plants or insects.

21) (Amended) Transformed cell expressing the mammalian neuronal amiloride-sensitive proton-activated cationic channels obtained by the method according to claim 18.

22) (Amended) Method for screening substances that are capable of modulating the activity of mammalian neuronal ionic channels, comprising contacting variable quantities of a substance to be tested with the cells according to claim 21 and measuring, using any suitable means, the effects of said substance on the currents of the amiloride-sensitive proton-activated cationic channels.

23) (Amended) Method according to claim 22, wherein said substance is capable of modulating the perception of acidity, with regard to nociception and taste transduction.

24) (Amended) Pharmaceutical composition comprising as active ingredient at least one protein constituting an ionic channel according to one of claims 1, 2, 3 and 5 or an antibody directed against said protein.

26) (New) Method according to claim 19, wherein the cell host is selected from among the prokaryotes or the eukaryotes and notably from among the bacteria, yeasts, or cells of mammals, plants, or insects.

27) (New) Transformed cell expressing the mammalian neuronal amiloride-sensitive proton-activated cationic channels obtained by the method of claim 19.

28) (New) Method for screening substances that are capable of modulating the activity of mammalian neuronal ionic channels, comprising contacting variable quantities of a substance to be tested with the cells according to claim 27 and measuring, using any suitable means, the effects of said substance on the currents of the amiloride-sensitive proton-activated cationic channels.

29) (New) Method according to claim 28, wherein said substance is capable of modulating the perception of acidity, with regard to nociception and taste transduction.

In the Abstract (clean copy as amended)

A protein constituting a mammalian neuronal cationic channel that is sensitive to amiloride and activated by protons, as well as the nucleic acid molecules coding this protein; and a method for screening substances that are capable of modulating the activity of mammalian neuronal ionic channels.

C9